

APPLICANTS: Peled et al.
U.S.N.: 09/986,897

Listing of Claims:

Claim 1 (currently amended): A An expanded hematopoietic cell population cultured of committed progenitor hematopoietic cells and/or non-differentiated, early hematopoietic progenitor cells, said expanded hematopoietic cell population obtained by ex vivo culturing in a culture medium under conditions permitting cells of said cell population to proliferate and, at the same time, reducing a capacity of said cells in utilizing copper, of seeded hematopoietic cells in a culture medium in the presence of a transition metal chelator,

said chelator having affinity for copper and present in an amount sufficient to inhibit differentiation while permitting expansion of said hematopoietic cells cell population in said culture medium,

and wherein said hematopoietic cells are hence expanded yet not further differentiated as compared to ex vivo seeded hematopoietic cells from which said expanded hematopoietic cell population developed expanded.

Claim 2 (currently amended): The expanded hematopoietic cell population of claim 1, wherein said cells are provided in said medium.

Claim 3 (currently amended): The expanded hematopoietic cell population of claim 1, wherein said cells are isolated from said medium.

Claim 4 (currently amended): A pharmaceutical composition comprising the expanded hematopoietic cell population of claim 1.

Claim 5 (currently amended): A pharmaceutical composition comprising the expanded hematopoietic cell population of claim 3.

Claim 6 (cancelled)

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Claim 7 (currently amended): The expanded hematopoietic cell population of claim 1 6, wherein said seeded cells are enriched for hematopoietic stem or progenitor cells.

Claim 8 (currently amended): The expanded hematopoietic cell population of claim 1 6, wherein said hematopoietic cells are derived from a source selected from the group consisting of peripheral blood, bone marrow and neonatal umbilical cord blood.

Claims 9-17 (cancelled)

Claim 18 (currently amended): The ~~cell~~ expanded hematopoietic cell population of claim 1 7, wherein said transition metal chelator is selected from the group consisting of polyamine chelating agents, ethylenediamine, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenepentamine, aminoethylethanolamine, aminoethylpiperazine, pentaethylenhexamine, triethylenetetramine-hydrochloride, tetraethylenepentamine-hydrochloride, pentaethylenhexamine-hydrochloride, tetraethylpentamine, captopril, penicillamine, N,N'-bis(3-aminopropyl) 1,3 propanediamine, N,N-Bis(2-aminoethyl)1,3 propane diamine, 1,7 dioxo 4,10-diaza-cyclododecane, 1,4,8,11-tetraaza-cyclo-tetradecane-5,7-dione, 1,4,7-triazacyclononane trihydrochloride, and 1-oxa-4,7,10-triazacyclododecane, 1,4,8,12-tetraaza-cyclopentadecane, 1,4,7,10-tetraaza-cyclododecane.

Claim 19 (currently amended) The expanded hematopoietic cell population of claim 17, wherein said culture medium ~~population~~ comprises nutrients and a cytokines.

Claim 20. (currently amended): The expanded hematopoietic cell population of claim 19, wherein said cytokines ~~are~~ is an early acting cytokines.

Claim 21 (currently amended): The expanded hematopoietic cell population of claim 20, wherein said early acting cytokines ~~are~~ is selected from the group consisting of stem cell factor, FLT3 ligand, interleukin-6, thrombopoietin and interleukin-3.

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Claim 22 (currently amended): The expanded hematopoietic cell population of claim 19, wherein said cytokines ~~are~~ is a late acting cytokines.

Claim 23 (currently amended): The expanded hematopoietic cell population of claim 22, wherein said late acting cytokines are is selected from the group consisting of granulocyte colony stimulating factor, granulocyte/macrophage colony stimulating factor and erythropoietin.

Claim 24 (cancelled)

Claim 25 (currently amended): A An expanded hematopoietic cell population cultured *ex-vivo* in a culture medium wherein said hematopoietic cell population is expanded yet not further differentiated and having a reduced intracellular copper content as compared to *ex-vivo* seeded cells from which said hematopoietic cell population developed originated.

Claim 26 (currently amended): The expanded hematopoietic cell population of claim 25, wherein said cells are provided in said medium.

Claim 27 (currently amended): The expanded hematopoietic cell population of claim 25, wherein said cells are isolated from said medium.

Claim 28 (currently amended): A pharmaceutical composition comprising the expanded hematopoietic cell population of claim 25.

Claim 29 (currently amended): A pharmaceutical composition comprising the expanded hematopoietic cell population of claim 27.

Claim 30 (currently amended): The expanded hematopoietic cell population of claim 25, wherein said cells are expanded yet not further differentiated as compared to said *ex-vivo* seeded cells from which said cell population developed originated.

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Claim 31 (cancelled)

Claim 32 (currently amended): The expanded hematopoietic cell population of claim 31 ~~25~~, wherein said seeded cells ~~are~~ originate from hematopoietic stem or progenitor cells.

Claim 33 (currently amended): The expanded hematopoietic cell population of claim 31 ~~25~~, wherein said hematopoietic cells are from a source selected from the group consisting of peripheral blood, bone marrow and neonatal umbilical cord blood.

Claim 34 (currently amended): The expanded hematopoietic cell population of claim 25, wherein said seeded cells ~~are enriched for~~ originate from CD34+ cells.

Claim 35 (cancelled)

Claim 36 (currently amended): The expanded hematopoietic cell population of claim 25, wherein said seeded cells ~~are~~ originate from neonatal umbilical cord cells.

Claims 37-41 (cancelled)

Claim 42 (currently amended): The expanded hematopoietic cell population of claim 25, wherein said expanded hematopoietic cell population is expanded in a culture medium comprises comprising a transition metal chelator having an affinity for copper, said chelator present in an amount sufficient to inhibit differentiation for reducing said intracellular copper content of said hematopoietic cells as compared to said *ex-vivo* seeded cells from which said cell population developed originated.

Claim 43 (currently amended): The expanded hematopoietic cell population of claim 42, wherein said transition metal chelator is selected from the group consisting of polyamine chelating agents, ethylenediamine, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenepentamine, aminoethylethanolamine, aminoethylpiperazine, pentaethylenehexamine,

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triethylenetetramine-hydrochloride, tetraethylenepentamine-hydrochloride, pentaethylenhexamine-hydrochloride, tetraethylpentamine, captopril, penicilamine, ~~N,N'-bis(3-aminopropyl)-1,3-propanediamine, N,N-Bis(2-aminoethyl)-1,3-propanediamine, 1,7-dioxo-4,10-diazacyclododecane, 1,4,8,11-tetraaza-cyclotetradecane-5,7-dione, 1,4,7-triazacyclononane trihydrochloride, and 1-oxa-4,7,10-triazacyclododecane, 1,4,8,12-tetraaza-cyclopentadecane, 1,4,7,10-tetraaza-cyclododecane.~~

Claim 44 (currently amended): The expanded hematopoietic cell population of claim 42, wherein said culture medium comprises nutrients and a cytokines.

Claim 45 (currently amended): The expanded hematopoietic cell population of claim 44, wherein said cytokines ~~are~~ is an early acting cytokines.

Claim 46 (currently amended): The expanded hematopoietic cell population of claim 45, wherein said early acting cytokines ~~are~~ is selected from the group consisting of stem cell factor, FLT3 ligand, interleukin-6, thrombopoietin and interleukin-3.

Claim 47 (currently amended): The expanded hematopoietic cell population of claim 44, wherein said cytokines ~~are~~ is a late acting cytokines.

Claim 48 (currently amended): The expanded hematopoietic cell population of claim 47, wherein said late acting cytokines ~~are~~ is selected from the group consisting of granulocyte colony stimulating factor, granulocyte/macrophage colony stimulating factor and erythropoietin.

Claims 49-50 (cancelled).

Claim 51. (newly added): The expanded hematopoietic cell population of claim 18, wherein said transition metal chelator is tetraethylenepentamine.

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Claim 52. (newly added): The expanded hematopoietic cell population of claim 51, wherein said transition metal chelator concentration is about 0.1 μM to about 100 mM.

Claim 53. (newly added): The expanded hematopoietic cell population of claim 52, wherein said transition metal chelator concentration is about 4 μM to about 50 mM.

Claim 54. (newly added): The expanded hematopoietic cell of claim 53, wherein said transition metal chelator concentration is about 5 μM to about 40 mM.

Claim 55. (newly added): The expanded hematopoietic cell population of claim 21, wherein said early acting cytokine is FLT3 ligand.

Claim 56. (newly added): The expanded hematopoietic cell population of claim 23, wherein said late acting cytokine is granulocyte colony stimulating factor.

Claim 57. (newly added): The expanded hematopoietic cell population of claim 43, wherein said transition metal chelator is tetraethylenepentamine.

Claim 58. (newly added): The expanded hematopoietic cell population of claim 57, wherein said transition metal chelator concentration is about 0.1 μM to about 100 mM.

Claim 59. (newly added): The expanded hematopoietic cell population of claim 58, wherein said transition metal chelator concentration is about 4 μM to about 50 mM.

Claim 60. (newly added): The expanded hematopoietic cell population of claim 59, wherein said transition metal chelator concentration is about 5 μM to about 40 mM.

Claim 61. (newly added): The expanded hematopoietic cell population of claim 46, wherein said early acting cytokine is FLT3 ligand.

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Claim 62. (newly added): The expanded hematopoietic cell population of claim 48, wherein said late acting cytokine is granulocyte colony stimulating factor.